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Multiple hemangiomas of the skin, liver and intestinal tract

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The hemangioma is one of the most common tumors in infants and children, lymphangioma seems to be less common. LAMPE and LATOURETTE [11] have reported that this type of tumor occurs in siblings in only 3% of cases, and in 61% the tumors are present at birth or appear within the first months.

It was observed relatively late that there exists a connection between hemangioma and thrombocytopenia. The first report on capillary hemangioma with accompanying thrombocytopenia and purpura, by KASBACH and MERRITT [8], dates from 1940. This combination, therefore, is often called "Kasbach-Merritt Syndrome". A similar case, in a boy, four years of age, was noted by RHODES and BORELLI [15], in 1944. SILVER et al. [18], in 1948 reported on a case of capillary and cavernous hemangioma with thrombocytopenic purpura. It was treated with roentgen irradiation, which caused temporary amelioration of the symptoms, but the patient finally succumbed to hemothorax with atelectasis of the lung and depression of the diaphragm. A reddish-purple hemangioma associated with thrombocytopenic purpura was reported in a newborn infant by SOUTHARD et al. [20], in 1951. This was at that time the fourth case of this complication in the literature. The authors suggested that a possible sequestration of thrombocytes, in the tumor, was the cause of the thrombocytopenia. Also in 1951 BOGEN and THURMAND [3], published a paper on the treatment of a six week old boy with hemangioma, thrombocytopenia and erythrocytopenia. They considered this condition to be rare. WEISSMAN and TAGNON [21], in 1953 added two more cases to the slowly mounting list of hemangiomas with thrombocytopenia. GOOD et al. [7], in 1955 in exploring three cases of hemangiomas associated with thrombocytopenia, showed these to be related. These workers made histological studies of biopsied material stained with Wright's and hematoxylin-eosin stain. It could be demonstrated that large numbers of platelets were sequestered and destroyed within the tumor. Thus, more credibility was added to the theory of SOUTHARD et al. [20]. Up to 1958 when SCHERZ et al. [17] published the case of a one year old girl with hem-

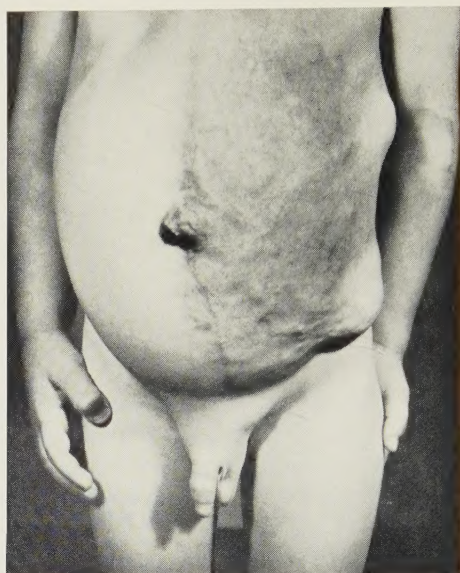


Fig. 1. Case 1, J. F. Hemangioma of left abdominal wall.

angioma and thrombocytopenic purpura, there seem to have been fourteen cases recorded in the literature. By the use of platelets labeled with radioactive chromium (Cr^{51}), KONTRAS et al. [9] in 1963, showed that platelets are sequestered in these tumors. In addition histological sections demonstrated the platelet thrombi.

It is the purpose of this paper to demonstrate two siblings with vascular tumors. One child who has the rare combination of hemangioma of the skin accompanied by thrombocytopenia as well as multiple hemangiomas of the liver and intestines, and the other child, of the same family, with a large lymphangioma of the cheek. In both children the tumors were noted at birth.

Case 1. J. F., male, 3 years of age, father age 43, mother 36, both healthy. The eighth child in a family of ten. All foregoing siblings are healthy. The birth weight was 4000 g. The entire pregnancy was normal and without any complications at birth. The child was born at home. The further development was normal.

At birth a large, bluish hemangioma of the left abdomen and flank was noted. This tumor appeared to be rather deep reaching and more prominent at its edges. A smaller, prominent hemangioma was noted on the back of the neck. At one year of age the angiomata were irradiated at the University's Dermatology Clinic, with the result that the tumors became more prominent.

At two years of age an anemia was observed, which improved on iron medication. From June 1960, the child appeared more pale and his condition became worse. He was tired and listless, with shortness of breath. He was sent to the Children's Hospital Basle for transfusion.

First admission. (August 4, 1960). – At an age of 3 years 4 months the child was ad-

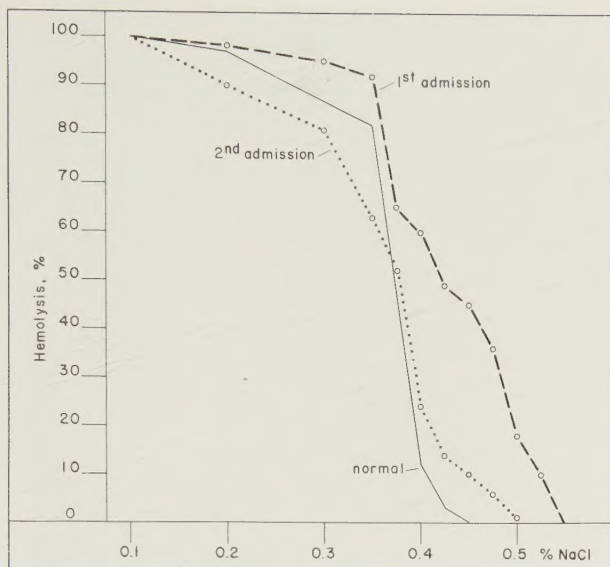


Fig. 2. Osmotic fragility curves.

mitted to the hospital. On admission he was listless, anorexic and had a tendency to diarrhea. The physical examination revealed his skin to be very pale. A large, prominent, bluish hemangioma covered the whole of the left abdomen and lower thorax (see Fig. 1). Another cherry-sized hemangioma was present at the base of the neck.

Laboratory findings. Hematology: The hemoglobin was 3.4 g%, RBC 2.01 millions. On the blood smear there was anisocytosis with micro-, plano- and poikilocytosis, some target cells and polychromatic macrocytes. The Price-Jones curve demonstrates an abnormal shift to the left, with greatly widened base and apex at 5 μ . MCH 17 $\mu\mu$ g. Reticulocytes 6.6%, thrombocytes were reduced to 76000, leukocytes 7400 (total). Osmotic fragility is increased and the curve obtained is much less steep than the normal (see Fig. 2). Bleeding and coagulation time was normal with a prothrombin of 66%. A bone marrow aspiration made at this time revealed a relatively cell rich marrow, normal leukopoiesis and increased erythropoiesis, with an erythroid/myeloid ratio of 1:1.7.

The stools were not visibly bloody, but gave a strongly positive benzidine test. This suggested that the blood loss, causing the anemia, was due to intestinal bleeding.

The serum values were found to be essentially normal, except for a diminished serum iron (34 μ g%). Bilirubin was 0.5 mg%. Total protein content was 5.8 g% and in electrophoresis the γ -globulin was somewhat low (8.5%). A direct Coombs-test was negative. Liver function tests: bromsulphalein retention, hippuric acid excretion, galactose tolerance test, and flocculation tests were all normal. The patient improved with a blood transfusion of 250 cm³. His hemoglobin rose to 5.9 g%. Further improvement was achieved by additional transfusions. The child was seen by an ophthalmologist in order to rule out hemangiomas of the eye. The both eye fundi were found to be normal. An i. v. pyelogram showed a normal renal pelvis and ureters. Several calcified areas were noted in the region of the liver. These concretions were about the size of cherry-pits. The exact location could not be determined on flat-plate films. A cholecystogram revealed



Fig. 3. Case 1, roentgenogram showing multiple phleboliths in the liver.

a normal gallbladder and ductus choledochus. The calcifications seemed to be in the liver itself (see Fig. 3). These concretions were thought to be phleboliths in the hemangiomas of the liver. No varices could be demonstrated in the esophagus. The filling of the venous system of the hemangioma of the abdominal wall did not demonstrate a connection between this hemangioma and those of the liver (see Fig. 4).

The condition of the patient was greatly improved at the beginning of September 1960. The ECG had become normal. Hemoglobin was 10 g%, erythrocytes 3.43 million, MCH 29 μg , leukocytes 7500 and thrombocytes 170000. At this time the child's parents insisted on taking him home and the patient was released from the Hospital, on September 3, 1960, in good general condition, correctly developed for his age.

Second admission. — On November 14, 1960 the child was again admitted to the Children's Hospital with a very severe iron deficiency anemia. At the time of admission the blood values were: hemoglobin 4.8 g%, erythrocytes 2.25 millions, MCH 21 μg , reticulocytes 4.8%. The blood smear was similar to that of the first admission. The osmotic fragility remained abnormally high (see Fig. 2). The Price-Jones curve was still abnormally shifted to the left with a broad base, but now the apex was at the normal value of 7 μ . Leukocytes were 5650 with a normal differentiation, and thrombocytes 121000. Coagulation studies: essentially normal findings were obtained. However, a deficient value was found for fibrinogen (120 mg%).

The serum iron was strongly reduced (30 $\mu\text{g}\%$). Electrophoresis showed normal serum proteins. A special diet was administered which would not interfere with the ben-zidine test and the test remained strongly positive on four separate occasions.

In order to locate accurately the foci of bleeding in the intestines, two barium meals were carried out by Prof. E. ZDANSKY, Chief of the Radiology Department of the University of Basle, School of Medicine. The following reports were made: No varices could be seen in the esophagus. In the pars horizontalis inferior duodeni, as well as in a few small bowel loops there were round and polygonal shadows, which were most likely



Fig. 4. Case 1, roentgenogram showing filling of the venous system of the hemangioma, with urographin.

hemangiomas. A second barium study revealed many round shadows in the ileum and also one in the jejunum. The patient was given two separate transfusions of 250 cm³ of blood and his hemoglobin rose to 8.8 g%. The child was much improved, but was still quite pale. He was then released from the hospital, after a further transfusion, on December 10, 1960, with a hemoglobin of 12.8 g%.

On January 24, 1961 and again on February 7, 1962 the patient underwent surgery, at the Surgery Department of the University of Basle. Small hemangioma nodules were removed from the small and large bowel; the multiple hemangiomas of both liver lobes were observed. A small nodule in the middle of the jejunum had already started an invagination. On March 12, 1962 the patient was released from the hospital and no further complications have been reported up to this time.

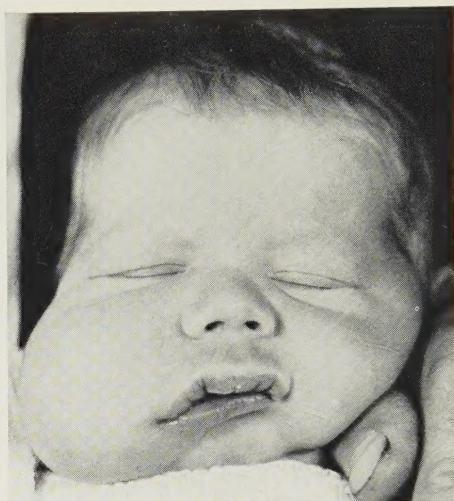


Fig. 5. Case 2. H. F. Cavernous lymphangioma of the right cheek.

Case 2. H. F. (brother of forementioned case). Born July 4, 1960 with a weight at birth of 4500 g. In this case as well, the pregnancy was without complication, as was the parturition. A somewhat increased amount of amniotic fluid was noted at birth. It was also noted, that the infant had an enormous swelling of the right cheek, which remained unchanged with the passage of four months time (see Fig. 5). At that time it was decided to admit the infant to the Surgery Department of the Children's Hospital Basle for operative therapy and histological clarification of the tumor. On admission, the right cheek was still found to be greatly swollen. On palpation of the swelling, it was found to have a doughy consistency. On the skin of the left side of the neck, just above the distal insertion of the musculus sternocleidomastoideus, an additional 3 cm long lead-pencil-thin tumor could be seen and palpated. The tumor was found to be of cystic consistency and was not fastened to the tissues below. The skin above both tumors was normal in color and temperature. The jaw and palate were symmetrical and no other abnormalities could be found. However, it was noted that the lower branch of the nervus facialis was not properly functioning and that the right corner of the mouth had a tendency to droop. The musculus orbicularis oculi was functioning and the eye could be closed tightly.

The infant was operated upon at two separate sittings, the following being the findings and results: The tumor was found to extend across the entire width of the cheek, from the corner of the eye to the ear and down to the edge of the lower jaw, as well as from skin above to the bone below. The growth was not sharply separated from the various tissues and had "infiltrated" part of the periosteum of the maxilla. Cysts of all sizes were found, and in the area of the zygomatic bone they were very small and not clearly defined from the rest of the tissue. The rest of the muscles showed definite signs of pressure atrophy. In the first surgical procedure the lymphangioma of the neck was totally removed, that of the cheek was resected to a great extent. In the second sitting more of the tumor of the cheek was removed, but it was now clear, that total resection was impossible. The histo-pathological diagnosis of the operative material (Prof. A. WERTHEMANN, Chief of the Pathology Department, University of Basle), was as follows: "Cavernous lymphangioma in the connective tissue of the neck and cheek."

The postoperative course was somewhat complicated by an infection of the woundbed, but it healed rapidly. The results of the operation were disturbed by the fact that the right corner of the mouth droops. On December 20, 1960, the child was released from the hospital. A third surgical procedure, for further resection and cosmetic correction, was planned for a later date.

Discussion

A great and confusing nomenclature exists, concerning the different types of hemangioma. A simple classification was suggested by BIVINGS [2], on observance of 165 patients with 200 hemangiomas, over a period of 22 years.

1. Simple hypertrophic type (strawberry mark). The most common in his series, which tends to regress spontaneously and seldom requires treatment.

2. Squamous-cell type: a) Naevus simplex. Faint marks most often seen on the occipital area of the head, and also on the face. These also tend to regress spontaneously and only cause concern of parents when they are on the face. b) Naevus flammeus (port-wine mark). These tend to remain permanently.

3. Cavernous type (naevus cavernosus). These usually lie subcutaneously and often require treatment.

4. Spider type (naevus araneus). These are small red-centered masses with radiating capillaries. They usually appear after infancy and will often persist for a long period of time, but they also tend to regress spontaneously.

The location of hemangiomas (NELSON [13]) are for the cavernous type: skin, bone, liver, skeletal muscles, and intestines. The naevus flammeus is usually at the side of the face and may correspond to the distribution of the trigeminal nerve branches. LAMPE and LATOURETTE [11] have reported observations of 510 patients, which allows good insight into the courses of these tumors. They found cutaneous involvement in 63% of cases, subcutaneous in 15% and both, cutaneous and subcutaneous, in 22%. The female/male ratio was 2,5:1. Similar lesions in siblings were found in 3% of the cases. 61% of the tumors were present at birth, or appeared within the first months of life. Early growth was noted in 85% of the cases. According to these authors, enlargement in the first few months is of prime importance in identifying those lesions, which will eventually regress spontaneously. The maximum size of the tumors is most often reached within the first year of life. 50% of the cases stopped growing before 6 months of age. A stationary period sets in, before involution begins. Changes in appearance usually start in the center of the lesion and go out towards the periphery. Early signs of involution appeared before 6 months of age in 16% of the cases, between 6 and 12 months in 65% and the remainder only began to regress after one year of age. In the majority of their cases the hemangiomas disappeared, or there were only slight traces of pigmentation by 5 years of age, regardless of therapy. Larger lesions required more time to regress.

Our case seems to take a unique place in the literature of hemangiomas, because it has the rare combination of a large hemangioma of the skin of the left abdominal wall and flank with associated thrombocytopenia, as well as multiple hemangiomas of both liver lobes and the small and large intestines. The hemangiomas of the liver caused no complications and the child had normal liver function tests, no esophagus varices and no pulsation or bruits were observed over the liver. Only a variable, slight hepatomegaly could be found. There were no cardiac abnormalities. The murmur, probably due to anemia, could no longer be heard after transfusion. Thus, there appear to be two forms of hemangiomas of the liver. One type, noted by AICARDI and NEZELOF [1] and EDMONDSON [6], has arteriovenous shunt formation in the tumors. This causes right heart strain and failure and often leads to death in the first 6 months. The other type remains asymptomatic throughout life and may only be a chance finding on a roentgenogram or at autopsy [16]. Our case would fall into this latter group. According to EDMONDSON [6], apart from liver-cell carcinoma, adrenal rest tumors and occasional solitary cysts, hemangiomas may show calcification on roentgenograms. He also feels that the finding of hepatomegaly with hemangiomas of the skin is practically diagnostic for liver hemangiomas. Both of these could be demonstrated in case 1, above. Our case also was complicated by intestinal bleeding, causing severe anemia on several occasions. The roentgen diagnosis of multiple hemangiomas of the small and large intestines was confirmed at laparotomy. Very few cases of hemangioma of the gut, with repeated intestinal hemorrhages, have been reported (COPPLE et al. [5] and SIMANDL et al. [19]). The usual therapy is operative removal, as was done in our case.

Lymphangiomas are much less frequently observed than hemangiomas (NELSON [13], KOOP [10]). They are, according to CHISHOLM [4], composed of various sized lymph spaces, containing amber colored lymph or white chylus fluid, and are lined with endothelial cells. The tumor is usually found at one focus, this most often being the neck, axilla, groin, mediastinum, and abdomen. The face and extremities are less often involved, and tumors are rarely observed in the orbit, eye, tongue and trunk. These authors have noted that the skin above the tumors is usually intact. This is in accordance with our case mentioned above. These tumors are often called "lymphangiectasia" in an effort to indicate that they are due to malformed lymph vessels and are not true tumors (CHISHOLM et al. [4], NELSON [13]). CHISHOLM et al. [4] found that these tumors, especially of the face, show little response to roentgen irradiation and will tend to recur after surgical excision. KOOP and MOSCHAKIS [10] reported on several cases of lymphangioma of the tongue and neck, treated with relative success by surgery and electrocoagulation. As our case has shown, it is very difficult or impossible to completely remove these lymphangiomas of the face, due to the distinct tendency to infiltrate, deform, and destroy, although they are microscopically benign. As to the

treatment of these perplexing tumors, I quote CHISHOLM et al. [4]: «Early radical surgery occasionally gets ahead of the process, but too often management constitutes multiple staged excisions in an effort to hold the lesions under control while the patient and his family learn to live with the deformity.»

Summary

Two cases of vascular tumors are presented. A case of hemangioma of the abdominal wall in a child of 3½ years, complicated by thrombocytopenia, anemia due to bleeding of hemangioma nodules of the intestines, and multiple, asymptomatic hemangiomas of the liver with calcification. Surgical excision of the intestinal hemangiomas halted the bleeding tendency from the gut. A review is also made of the previous literature on this tumor and its complications. Only 20 odd cases of this cause of hemorrhage and some 30 cases of hemangioma with thrombocytopenia have been reported. A second case, tenth child in the same family as the above mentioned, showed a large lymphangioma of the cheek. The problematics of this tumor, as well as the difficulty of its complete surgical resection are discussed.

Zusammenfassung

Bei einem 3½-jährigen Knaben besteht ein Hämangiom der Bauchdecke, das mit Thrombocytopenie, multiplen kalzifizierten asymptomatischen Leberhämangiomen und Anämie einhergeht, letztere bedingt durch Blutungen aus hämangiomatösen Knötchen des Darms. Nach chirurgischer Entfernung der intestinalen Hämangiome hörten die Blutungen aus dem Darme auf. Bis jetzt sind erst 20 Fälle mit dieser Art Hämorrhagie und etwa 30 Fälle von Hämangiomen mit Thrombocytopenie beschrieben worden. Ein Bruder des Knaben, das zehnte Kind derselben Familie, zeigt ein großes Lymphangiom der Wange. Die Problematik und die Schwierigkeit der vollständigen chirurgischen Entfernung werden diskutiert.

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